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## Risk factors and histomorphological patterns of female patients suspected of breast cancer attending Kisii Teaching and Referral Hospital, Kenya

Job Marege Anunda, Collins Ouma, Bernard Guyah & Samwel Otieno

Department of Biomedical Sciences, Maseno University, Kenya Corresponding author: Job Marege Anunda jomanunda@yahoo.com jp https://orcid.org/0009-0001-8880-3291

Abstract

**Background:** Breast cancer is a significant public health concern globally, and it is the leading diagnosed cancer among females. In Kenya, breast cancer accounts for 25.6% of all female cancer cases and presents with a high incidence of late-stage diagnoses. Previous studies have shown that risk factors for breast cancer vary in their associations with histomorphological patterns.

**Objectives:** This study aimed to determine the histomorphological characteristics and patterns of breast cancer in female patients suspected of having breast cancer at Kisii Teaching and Referral Hospital (KTRH), establish associations between these risk factors and the histomorphological patterns, and identify the most significant risk factors among female patients suspected of breast cancer attending KTRH.

**Methods:** A retrospective cross-sectional study was conducted at KTRH, reviewing 194 female patients' breast lump biopsies collected between September 2022 and August 2023. Data from pathological slides and hospital records were analyzed using IBM SPSS software version 28, with descriptive statistics and multinomial logistic regression applied to identify significant risk factors associated with histomorphological patterns of breast cancer.

**Results:** The mean participant age was 39.53±17.47 years, with 23.7% being nulliparous. Most participants had a primary level of education (37%), and the majority had no history of smoking

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(92.8%) as well as alcohol consumption (78.9%). The most common histomorphological pattern was fibroadenoma (33.0%), followed by invasive ductal carcinoma (21.1%). Benign conditions were diagnosed in 66.5% of cases, while 33.5% were malignant. A significant association was found between age ( $\chi^2$ =3.872, df=4, p≤0.0001); parity ( $\chi^2$ =23.616, df=3, p≤0.0001), history of cancer ( $\chi^2$ =4.204, df=1, p=0.003), and histomorphological patterns. Parity was significantly associated with all tumor types (ductal; OR=2.312, 95% CI=1.546-3.458, p<0.0001), (lobular; OR=2.919, 95% CI=1.190-7.159, p=0.019) and (mixed; OR=2.781, 95% CI=1.217-6.358, p=0.015).

**Conclusions:** This study identified a high incidence of late-stage breast cancer diagnoses at KTRH, underscoring the need for enhanced education and screening programs. Socio-demographic factors, particularly parity and age, significantly influence breast cancer histomorphological patterns. These findings inform targeted public health interventions and policy development to reduce breast cancer morbidity and mortality in Kenya.

Keywords: benign, breast cancer, histomorphological patterns, malignant, risk factors

#### **Public Interest Statement**

Breast cancer is a principal cause of cancer deaths in low-income countries, affecting women of all ages, with risk increasing with age. Stigma often leads to poor health-seeking behavior. In Kisii, patient-related factors obstruct diagnosis and management. These include socio-cultural beliefs, delayed reporting, lack of cancer education, denial, and economic challenges. Consequently, most breast cancer cases are diagnosed at advanced stages, complicating treatment and resulting in high mortality.

#### Introduction

Breast cancer is a major public health concern that has been extensively researched over the past decades. Being the leading cause of new cases of cancer at 11.7% and 24.5% of cancer cases in females, the disease burden informs that more research and public health intervention needs to be intensified. In Kenya, breast cancer is the leading cause of all cancers, contributing to 16.1% as of 2020 (GLOBOCAN, 2023). It contributes 25.6% of all cancers in females in all new cases (GLOBOCAN, 2023). With an incidence of 41.0% and a mortality of 19.4%, breast cancer remains a disease of concern that requires attention from resources and skilled professionals (GLOBOCAN, 2023). Breast cancer in Kenya correlates with the situation in Africa, with 16.8% for all cancers and 29.5% for females (GLOBOCAN, 2023).

Breast cancer is a public health problem in Kisii Teaching and Referral Hospital (Mong'are et al., 2022). It is reported that breast cancer cases contributed to 22% of all the breast cases reported at the breast oncology clinic(Bahaty & Kenneth, 2012). The majority of the cases of breast cancer, which contributed to 79%, presented to the clinic at advanced stages (stages 3 and 4). The main reasons for late presentation included a lack of knowledge and financial constraints hindering early health seeking; some were treated at peripheral facilities and reassured without biopsy, and some also visited herbalists (Bahaty & Kenneth, 2012).

Kisii Teaching and Referral Hospital also serves the nearby counties, with Nyamira County being the chief dependent. Homa Bay County recorded lower screening levels of 7.8%. Furthermore, no cancer center exists in Homa Bay (Odhiambo et al., 2023). The breast cancer prevalence and incidence in Bomet County are not documented, yet morbidities and mortalities attributable to it are reported (Chelangat et al, 2019). An unpublished report from one mission hospital in Bomet County reports breast cancer as the second cancer among women, estimated at 60 cases per 1700 in 2015 (Eddis et al., 2019). Unless urgent action is taken to advance breast cancer screening and diagnosis, breast cancer will compound Kenya's disease burden and increase poverty and gender inequalities (MoH, 2021).

This study aimed to examine risk factors and histomorphological patterns of suspected malignant breast lumps in female patients at Kisii Teaching and Referral Hospital. The social demographic characteristics of the study participants were further associated with the histomorphological patterns and defined possible risk factors, which will inform the decision-making process and development of new policies to curb the surge of breast cancer cases.

#### Methods

#### Study Area

The study was done at Kisii Teaching and Referral Hospital. The hospital offers oncology services, a histology laboratory, functional surgical departments, a consultant oncoplastic breast, and a general surgeon, all of which are key in cancer diagnosis and management. Counties bordering KTRH are Nyamira, Narok, Migori, Bomet and Homabay. Most patients were streaming into Kisii Teaching and Referral Hospital for oncologic reviews and other services. The catchment was estimated to be over 1.5 million. The gynecology clinic booking stood at an average of 15 clients per week with at least six breast lumps for biopsy removal and processing at the laboratory.

#### Study Design

A retrospective cross-sectional study design with both primary and secondary data was used. Primary data was obtained from reviewed pathological slides, and secondary data was obtained from the hospital records. The study targeted all female breast lump biopsies collected at the Kisii Teaching and Referral Hospital gynecology clinic. Purposive sampling was used to select tissue blocks collected between September 1, 2022, and August 31, 2023. The following checklist was used with the rejection of block in case any of the lists in the checklist were not met. Purposive sampling of all eligible archived tissue blocks within one year was done. The study data was coded to obscure identity. All information was entered into a password-protected computer spreadsheet, cleaned, and exported into IBM SPSS software version 28 for analysis (SPSS, 2022). Descriptive statistics were used to test for the significance of different variables. All p-values <0.05 were considered statistically significant.

#### **Inclusion** Criteria

All female patients of any age with breast lumps whose breast lumps samples were collected and stored in the Kisii Teaching and Referral Hospital pathology department were included in the study.

#### **Exclusion** Criteria

Participants whose file records and tissues were not available.

#### Results

#### Characteristics of Study Participants

The study enrolled a total of 194 women who met the inclusion criteria. In **Table 1a**, the sociodemographic characteristics are shown. The mean age of the study participants was  $39.53\pm17.467$ , indicating an extensive age range of 76. The mean weight was  $61.691\pm12.682$ . Most of the participants had a primary level of education (73). Most women were nulligravida; parity of zero (n=46/23.7%). The majority of the women were non-smokers in terms of cigarette smoking (92.8%), while 78.9% did not take alcohol. Women who used hormonal contraceptives were 67(34.5%), while the majority, 127(65.5%), were reported to have not been exposed to contraceptives.

Characteristic	Condition	Frequency	Percent	Valid Percent
Parity	0	46	23.7	23.7
	1	23	11.9	35.6
	2	25	12.9	48.5
	3	29	14.9	63.4
	4	18	9.3	72.7
	5	26	13.4	86.1
	6	13	6.7	92.8
	7	6	3.1	95.9
	8	6	3.1	99.0
	9	1	0.5	99.5
	14	1	0.5	100.0
Smoking cigarette	NO	180	92.8	92.8
	YES	14	7.2	100.0
Alcohol consumption	NO	153	78.9	78.9

Table 1a: Summary of Socio-demographic Characteristics of the Study Participants

	YES	41	21.1	100.0
Hormonal contraceptives	NO	127	65.5	65.5
	YES	67	34.5	100.0

SD; standard deviation

Table 1b presents a summary of the histomorphological patterns of study participants. The majority of patients were diagnosed with fibroadenoma, 64(33.0%), followed by invasive ductal carcinoma at 41(21.1%), with only one patient presenting with lactating adenoma, 1(0.5%). Fibrocystic changes were diagnosed at 20(10.3%) with mastitis cases reported at 16(8.2%).

#### Table 1b: Distribution of Age and Weight

Variable	Frequency	Minimum Value	Maximum Value	Mean	Std. Deviation
Age	194	15	91	39.53	17.467
Weight (Kg)	194	37.0	93.0	61.691	12.6824

The mean weight was  $61.691\pm12.682$ . The mean age of the study participants was  $39.53\pm17.467$ , indicating an extensive age range of 76.

Table 1c presents the distribution of histomorphological patterns among 194 breast lesion cases. Fibroadenoma was the most frequent condition, accounting for 33.0% of cases, followed by invasive ductal carcinoma at 21.1%. Other notable conditions include fibrocystic changes (10.3%) and mastitis (8.2%). Less common diagnoses include high-grade cell carcinoma, lactating adenoma, and ductal carcinoma in situ.

	Characteristics	Frequency	Percentage	Cumulative %
Histomorphological	Breast lipoma	6	3.1	3.1
pattern	Ductal carcinoma In Situ	2	1.0	4.1
	Ductal ectasis	11	5.7	9.8
	Fibroadenoma	64	33.0	42.8
	Fibrocystic changes	20	10.3	53.1
	Galactocele	4	2.1	55.2
	High-Grade cell Carcinoma	1	0.5	55.7
	Inflammatory Breast cancer	6	3.1	58.8
	Intraductal papilloma	3	1.5	60.3
	Invasive Ductal Carcinoma	41	21.1	81.4
	Invasive Lobular Carcinoma	7	3.6	85.1
	Lactating adenoma	1	0.5	85.6
	Lobular Carcinoma In Situ	2	1.0	86.5
	Mastitis	16	8.2	94.8
	Paget's Disease of Breast	2	1.0	95.8
	Phyllodes tumor	5	2.6	98.5
	Triple Negative Breast Cancer	3	1.5	100.0
	Total	194	100.0	100.0

Table 1c: Histomorphological characteristics of the study participants

The clinical characteristics of the study participants are presented in **Table 1d**. The majority of women were diagnosed with benign conditions of the breast, with 129(65.5%) and 65(33.5%) presenting with malignant conditions. History of cancer was reported at 8 (4.1%), with most of the patients reporting reporting no history of cancer, 186(95.9%). Within those who were diagnosed with malignant conditions of cancer, 22 patients (11.1%) were diagnosed with Breast cancer stage IV, 32 (16.5%) with stage III, and 9 (4.6%) with stage II. In terms of the grade of cancer, 35(18.0%) were reported with grade II, while 21(10.8%) presented with grade III. Only 9(4.6%) of the women presented with grade I breast cancer.

History of Cancer	NO	186	95.9	95.9
	YES	8	4.1	100.0
Cancer Condition	Benign	129	66.5	66.5
	Malignant	65	33.5	100.0
Cancer Stage	0	1	0.5	0.5
	1	1	0.5	1.0
	2	9	4.6	5.7
	3	32	16.5	22.2
	4	22	11.3	33.5
	N/A	129	66.5	100.0
Cancer Grade	1	9	4.6	4.6
	2	35	18.0	22.6
	3	21	10.8	33.5
	N/A	129	66.5	100.0

Table 1d: Clinical Characteristics of Study Participants

N/A denotes a benign cancer condition that cannot be staged or graded. Only malignant conditions are graded and staged.

Figure 1 below shows that most participants had attained primary (73/37.63%) in terms of their education level.



Figure 1. Education Level Distribution

Figure 2 below displays the distribution of various histomorphological patterns of breast conditions, with Fibroadenoma being the most common at 33.0%, followed by Invasive Ductal Carcinoma at 21.1%. Less common conditions include Fibrocystic changes (10.3%), Mastitis (8.2%), and other rare conditions like Lactating Adenoma (0.5%)





# Objective 1: The histomorphological characteristics and patterns of breast cancer in female patients suspected of breast cancer attending Kisii Teaching and Referral Hospital.

In this study, the most common type of histomorphological characteristic was "other tumors" 111(60.3%). The ductal type was presented in 59(30.4%) patients, while the lobular type was reported in only 9(4.6%) of the patients enrolled. Most (57.2%) of the "Other tumors" were benign, with 3.1% malignant. The mixed type, 9(100.0%), presented with malignant conditions. The majority (72.9%) of the ductal tumor types were malignant. The results are presented in Table 4.2.

Histomorphological characteristics	Cancer co	Total		
Benign		Malignant		
Ductal	Count	16	43	59
	% within	27.1%	72.9%	100.0%
- Ductal Carcinoma In Situ	% of	8.2%		30.4%
- Ductal Ectasia,	Total			
- Invasive Ductal Carcinoma			22.2%	
- Paget's disease of the breast				
- Intraductal Papilloma				
Lobular	Count	2	7	9
	% within	22.2%	77.8%	100.0%
- Invasive Lobular Carcinoma	% of	1.0%	2 ( 0/	4.6%
- Lobular Carcinoma In Situ	Total		3.6%	

Table 4.2:	Characteristics	of histomorphological	l conditions	of patients	attending	Kisii	Teaching	and
Referral H	lospital							

Mixed	Count	0	9	9
	% within	0.0%	100.0%	100.0%
- Inflammatory Breast Cancer	% of	0.0%	4 ( 0/	4.6%
- Triple Triple-negative breast cancer	Total		4.6%	
Others	Count	111	6	117
	% within	94.9%	5.1%	100.0%
- Breast Lipoma	% of	57.2%		60.3%
- Fibroadenoma	Total			
- Fibrocystic changes				
- Galactocele				
- High-Grade Spindle Cell Carcinoma			3.1%	
- Lactating Adenoma				
- Mastitis				
- Phyllodes Tumor				
Total	Count	129	65	194
	% of	66.5%	22 50/	100.0%
	Total		<i>33.</i> 3%	

Table legend: A mixed tumor type means it affects both parts of the ducts and lobules. "Others' means those tumors that were neither in the three categories (ductal, lobular, or both ductal and lobular).

## Objective 2: The associations between risk factors and histomorphological patterns in female patients suspected of breast cancer attending KTRH.

A total of 194 patients were diagnosed with breast lesions. There is a wide range of ages among the women in the current study, between 15 and 91 years old, with a median age of 37. The average age was  $39.53\pm17.467$ . The weight range spans from 37 kg to 93 kg, with a median weight of 61.5 kg. The average weight was  $61.691\pm12.682$ . More than half of the participants (55.57%) were below the age of 40 years. Using the independent chi-square test of association, there was a statistical association between age category with risk of tumors ( $\chi^2=3.872$ , df=4, p <0.0001); parity ( $\chi^2=23.616$ , df=3, p = <0.0001), history of cancer ( $\chi^2=4.204$ , df=1, p = 0.003), histomorphological characteristics ( $\chi^2=194.000$ , df=16, p <0.0001) and level of education ( $\chi^2=9.488$ , df=3, p = 0.001). On the other hand, alcohol consumption; ( $\chi^2=2.503$ , df=1, p = 0.114) were not associated with cancer conditions. The results are presented in Table 4.3.

Table 4.3: Association	between	demographic,	clinical, a	and histologica	al characteristics	of study	partici-
pants							

Characteristics	Cancer condition		Chi-square	p-value	
			value (df)		
	Benign Malignant				
	(n=129)	(n=65)			
Age (mean±SD)	39.53±17.46	7			
Weight (mean±SD)	61.691±12.682				
Age (years)					

<40	85(78.7)	23(21.3)	20.203(4)	
40-49	18(58.1)	13(41.9)		
50-59	10(43.5)	13(56.5)		<0.0001
60-69	13(59.1)	9(40.9)		
≥70	3(30.0)	7(70.0)		
Total	129(66.5)	65(33.5)		
Cigarette Smoking	·	·		<u>.</u>
NO	117(65.0))	63(35.0)	2.502(1)	0.114
YES	12(85.7)	2(14.3)		
Total	129(66.5)	65(33.5)		
Hormonal Contraceptives	·			Γ.
No	84(66.1)	43(33.9)	0.021(1)	0.886
YES	45(67.2)	22(32.8)		
Total	129(66.5)	65(33.5)		
Alcohol Consumption	·	·		<u>.</u>
NO	102(66.7)	51(33.3)	0.010(1)	0.922
YES	27(65.9)	14(34.1)		
Total	129(66.5)	65(33.5)		
Parity	·			<u>n</u>
0	42(91.3)	4(8.7)	23.616(3)	<0.0001
1-3	52(67.5)	25(32.5)		
4-6	30(52.6)	27(47.4)		
≥7	5(35.7)	9(64.3)		
Total	129(66.5)	65(33.5)		
History of Cancer	·			<u>r</u>
NO	121(65.1)	65(34.9)	4.204(1)	0.003
YES	8(100.0)	0(0.0)		
Total	129(66.5)	65(33.5)		
Histopathological Patterns				

Breast lymphoma	6(100.0)	0(0.0)	194.000(16)	<0.0001
Ductal carcinoma In Situ	2(100.0)	0(0.0)		
Ductal Ectasia	11(100.0)	0(0.0)		
Fibroadenoma	64(100.0)	0(0.0)		7
Fibrocystic changes	20(100.0)	0(0.0)		
Galactocele	4(100.0)	0(0.0)		
High-grade spindle cell carcinoma	0(0.0)	1(100.0)		
Inflammation breast cancer	0(0.0)	6((100.0)		
Intraductal papilloma	3(100.0)	0(0.0)		
Invasive ductal carcinoma	0(0.0)	41(100.0)		
Invasive lobular carcinoma	0(0.0)	7(100.0)		
Lactating adenoma	1(100.0)	(090.0)		
Lobular carcinoma In Situ	2(100.0)	0(0.0)		
Mastitis	16(100.0)	0(0.0)		
Paget's disease of the breast	0(0.0)	2(100.0)		
Phyllodes tumour	0(0.0)	5(100.0)		
Triple-negative Breast cancer	0(0.0)	3(100.0)		
Total	129(66.5)	65(33.5)		_
Education Level		•	°	
Primary	28(38.36)	45(61.64)	9.488(3)	0.001
Secondary	45(81.82)	10(18.8)		
Tertiary	56(84.85)	10(15.15)		
Total	129(66.5)	65(33.5)		
Histomorphological Characteristics				
Ductal	16(27.1)	43(72.9)	109.128(3)	0.001
Lobular	2(22.2)	7(77.8)		
Mixed	0(0.0)	9(100.0)		
Others	111(94.9)	6(5.1)		
Total	129(66.5)	65(33.5)		

SD = standard deviation

#### Objective 3: Risk factors among female patients suspected of breast cancer attending KTRH.

The binary logistic regression model was used to predict the most significant risk factors associated with histological characteristics of breast cancer for the first significant variables with the chi-square test. The outcomes show that a history of cancer was significantly linked with breast cancer (OR=4.634, 95% CI=1.017-7.706, p=0.040), where those who had a history of cancer were more than four times more likely to progress into breast cancer. The other factor that was associated with breast cancer was histomorphological characteristics (lobular; OR=5.198, 95% CI=4.058-9.885, p=0.001 and (ductal;

OR=6.387, 95% CI=5.745-8.662, p=0.001). The results are shown in Table 4.4.

	Cancer condition				
Characteristics	Benign	Malignant	OR	(95%CI)	p-value
	(n=129)	(n=65)			
Age (years)		-		<u>.</u>	
<40	69(63.9)	39(36.1)	Ref.		
40-49	21(67.7)	10(32.3)	0.802	0.052-12.539	0.802
50-59	17(73.9)	6(26.1)	0.679	0.037-12.510	0.679
60-69	17(73.9)	5(22.7)	0.438	0.020-9.663	0.601
≥70	5(50.0)	5(50.0)	0.587	0.027-12.586	0.733
Parity		·	2	n	
0	42(91.3)	4(8.7)	Ref.		
1-3	52(67.5)	25(32.5)	1.077	0.210-5.512	0.952
4-6	30(52.6)	27(47.4)	1.052	0.203-5.463	0.929
≥7	5(35.7)	9(64.3)	0.265	0.031-2.236	0.222
History of Cancer					
NO	121(65.1)	65(34.9)	Ref.		
YES	0(0.0)	8(100.0)	4.634	1.017-7.076	0.040
Education Level					
Primary	97(61.1)	62(38.9)	Ref.		
Secondary	10(100.0)	0(0.0)	3.543	0.026-8.915	0.614
Tertiary	22(88.0)	3(12.0)	0.580	0.094-3.571	0.557
Histological Characteristics					
Others	111(94.9)	6(5.1)	Ref.		
Ductal	16(27.1)	43(72.9)	6.387	5.745-8.662	0.001
Lobular	2(22.2)	7(77.8)	5.198	4.058-9.885	0.001
Mixed	0(0.0)	9(100.0)	0.897	0.210-5.997	0.999

Table 4.4: Association between risk factors and histopathological patterns in women suspected of breas
cancer attending KTRH

Ref. denotes the reference category.

#### Discussion

Breast cancer is the most frequently diagnosed cancer among women in the world, as well as the dominant root of death from malignant tumors. The incidence of breast cancer is continually growing in all regions of the world (Smolarz et al., 2022). This current surge in breast cancer cases necessitates a need for more research and resource allocation to curb this menace. It is for this reason that despite the progress in its detection and treatment, which explains improved mortality rates, it seems necessary to improve the awareness and early diagnosis of breast cancer (Smolarz et al., 2022).

The study involved 194 women, providing a broad spectrum of socio-demographic characteristics relevant to breast cancer research. The various breast archived tissue blocks were analyzed for the various histomorphological patterns. The study revealed that a significant majority of the participants were diagnosed with benign breast conditions (65.5%), while 33.5% had malignant conditions. This unveiled a high incidence of breast cancer cases at 33.5% at Kisii Teaching and Referral Hospital, representing

Kisii County and the neighboring counties seeking oncology services at the facility, compared to the national tally of 16.1% (GLOBOCAN, 2023). According to the MoH publication of 2020, the estimates were, however, thought to be higher given the many unreported and unaccounted cases (MoH, 2020).

In the year 2012, it was reported that breast cancer cases contributed to 22% of all the breast cases reported at the breast oncology clinic (Bahaty & Kenneth, 2012). The majority of the cases of breast cancer, which contributed to 79%, presented to the clinic at advanced stages (stages 3 and 4). The main reasons for late presentation included a lack of knowledge and financial constraints hindering early health seeking; some were treated at peripheral facilities and reassured without biopsy, and some also visited herbalists (Bahaty & Kenneth, 2012). With improved awareness and breast cancer campaigns, more people have been visiting the facilities, leading to even higher incidences of breast cancer.

Among those with malignant conditions, a notable percentage were diagnosed at late stages: Stage III (49.2%) and Stage IV (34.0%), making a total of 83.2% diagnosed at late stage. Compared to other studies, it was reported that 77% of breast cancer cases were diagnosed with advanced disease(Matheka et al., 2023). Late-stage diagnoses are associated with poorer prognoses and emphasize the necessity of improved early detection and screening programs (Erratum: Global Cancer Statistics, 2020). The grading of breast cancer showed that most malignant cases were of Grade II (53.9%) and Grade III (32.3%). Grade II and III cancers are more aggressive and have a worse prognosis compared to Grade I, which constituted 13.8% of the cases (Elston & Ellis, 1991).

Some benign breast conditions are capable of undergoing neoplasia to become malignant tumors (Kar & Arora, 2023). For instance, fibroadenoma has in the past been reported to have undergone neoplasm to become a malignant tumor over time. However, it is a rare condition that accounts for 0-2% of the cases of malignancy (Kar & Arora, 2023). In this study, some cases were previously diagnosed as fibroadenoma in the previous clinical visits but were later confirmed to be malignancy. This calls for being vigilant with the benign conditions and high suspicion index to avoid an advance in breast disease. Late diagnosis has always been attributed to a lack of awareness. Women with secondary and tertiary education levels showed lower frequencies of malignant conditions, possibly due to improved health literacy and access to healthcare services (DeSantis et al., 2019). The majority of women with secondary or tertiary levels of education were mainly diagnosed with fibroadenoma or other benign breast conditions as opposed to their counterparts with a primary level of education who were diagnosed primarily with late-stage breast tumors. This health-seeking outcome suggested a high level of awareness and suspicion by those with secondary or tertiary levels of education, prompting them to seek early medical intervention in cases of any breast abnormality.

Economic vulnerability limits access to cancer care, leading to delayed diagnoses and poorer prognoses(Haier & Schaefers, 2022). Poverty and lack of economic resources are critical reasons for the reduced uptake of screening services and cancer diagnosis. Patients from less privileged families usually take too long to seek healthcare due to financial constraints, thereby seeking help when the disease is at advanced stages. Late health-seeking behavior usually leads to poor health outcomes.

# The histomorphological characteristics and patterns of breast cancer in female patients suspected of breast cancer attending Kisii Teaching and Referral Hospital.

The various histomorphological patterns that were discovered included breast lipoma, Ductal Carcinoma In Situ (DCIS), Ductal ectasia, Fibroadenoma, Fibrocystic changes, Galactocele, High-Grade Cell Carcinoma, Inflammatory Breast Cancer, Intraductal Papilloma, Invasive Ductal Carcinoma (IDC), Invasive Lobular Carcinoma (ILC), Lactating Adenoma, Lobular Carcinoma In Situ (LCIS), Mastitis, Paget's Disease of the Breast, Phyllodes Tumor, and Triple Negative Breast Cancer. Fibroadenoma was the most prevalent diagnosis (33.0%), followed by invasive ductal carcinoma (21.1%). Fibroadenomas are benign tumors common in younger women, while invasive ductal carcinoma is the most frequent type of breast cancer, typically occurring in older women (Lima et al., 2021).

The histomorphological diversity observed in this study emphasizes the importance of accurate histopathological diagnosis in managing breast lumps. The histomorphological patterns show a wide range of both benign and malignant breast conditions, with fibroadenoma being the most common benign condition and invasive ductal carcinoma being the most prevalent malignant condition(Laxman et al., 2018). The clinical characteristics indicate a significant number of participants with advanced-stage and high-grade cancers, suggesting a need for early detection and improved diagnostic methods. Invasive ductal carcinoma, in concurrence with other studies, is the most prevalent form of breast cancer(Waks & Winer, 2019).

# The associations between risk factors and histomorphological patterns in female patients suspected of breast cancer attending KTRH.

Risk factors are generally modifiable and non-modifiable (Smolarz et al., 2022). Modifiable risks include hormonal factors, lifestyle (alcohol consumption, smoking, obesity, and physical inactivity), and reproductive factors (parity). Non-modifiable factors include age, gender, family history, genetic predisposition, and reproductive history (Smolarz et al., 2022). Environmental factors such as radiation exposure have also been linked to incidences of cancer in general. These risk factors have previously been positively associated with the risk of breast cancer development in humans (Smolarz et al., 2022). Gender is a non-modifiable risk factor that is considered the most potent risk factor for breast cancer. It is estimated that about 99% of breast cancer cases are women, with only 1% of the cases being men (Smolarz et al., 2022). This high incidence of breast cancer. However, in this study, gender was not considered since women are considered the primary risk group.

Age is an essential non-modifiable risk factor for breast cancer. Research has shown that the incidence of breast cancer increases with progressing age, particularly in individuals aged 40 and older (Sun et al., 2017). In 2016, approximately 99.3% of breast cancer-related deaths in the United States occurred in women over 40, while 71.2% of these deaths were in women over 60 (Siegel et al., 2018). In this study, there was a significant association between age and breast cancer risk. Age had a p-value of 0.000, which indicates a strong association. This proved that age is one of the critical risk factors for breast cancer. Women aged 40-49 and 50-59 exhibited higher rates of malignant conditions compared to younger age groups, which is consistent with the usual age distribution for breast cancer incidence (Islami et al., 2022).

A family history of cancer is another risk factor for breast cancer. It is reported that only a small percentage of breast cancers, around 5-10%, are hereditary (Smolarz et al., 2022). The most well-known mutations associated with breast cancer are in the BRCA1 and BRCA2 genes (Mehrgou & Akouchekian, 2016). These mutations are found in about 3-5% of patients diagnosed with cancer, and carriers have an estimated tenfold increased risk of developing breast cancer(Collaborative Group on Hormonal Factors in Breast Cancer, 1996). This study found a significant association between a history of cancer and breast cancer incidence, with a p-value of 0.003. This significant relationship highlights the importance of cancer history as a major risk factor for breast cancer, aligning with the findings of other studies.

Hormonal factors like the use of hormonal contraceptives have been widely linked to incidences of breast cancer. Studies have shown that estrogen exposure and early menarche pose more risk for developing breast cancer(Smolarz et al., 2022). Moreover, it was clear that early first menstruation was associated with an increased risk of developing breast cancer, similar to the impact of late menopause. Each additional year of delayed menopause raised the relative risk by 2.9%. Menopause occurring after age 54 was considered late and doubled the risk of breast cancer compared to menopause occurring before age 45 (Smolarz et al., 2022).

Lifestyle is one of the modifiable risk factors for breast cancer. They include alcohol consumption, obesity, physical inactivity, and cigarette smoking (Smolarz et al., 2022). In this study, however, there

were insufficient existing records of alcohol consumption, obesity, physical inactivity, and smoking, hence, weaker association with breast cancer. Many studies suggest a link between alcohol consumption and a higher risk of breast cancer (Khushalani et al., 2020; Kim et al., 2017; Martin et al., 2018; Meyer et al., 2019; Smolarz et al., 2022). Lack of physical activity along with obesity raises the risk of developing breast cancer, regardless of menopausal status. Additionally, various studies have shown that being overweight or obese is linked to a poorer prognosis for breast cancer patients both before and after menopause (Smolarz et al., 2022; Suzuki et al., 2009).

Parity was significantly associated with breast cancer risk. These findings suggest a complex relationship between reproductive factors and the type of breast cancer, with parity exerting differential effects on various histomorphological patterns. Higher parity showed a protective effect against certain types of breast cancer, which is consistent with previous findings (Collaborative Group on Hormonal Factors in Breast Cancer, 2002). Nulliparity was the most common parity status (23.7%), signifying that most participants had not experienced pregnancy. This is an important consideration, as nulliparity has been allied to a higher risk of certain types of breast cancer, including hormone receptor-positive breast cancer (Collaborative Group on Hormonal Factors in Breast Cancer, 2002). It is, however, contentious as various studies have suggested multiple outcomes, some documenting high parity as a risk for breast cancer while others linking nulliparity or lower parities as a risk for breast cancer.

#### Risk factors among female patients suspected of breast cancer attending KTRH.

Previous studies have highlighted parity, age, lifestyle history of cancer, and hormonal contraceptives to be some of the most critical risk factors for developing breast cancer (Sun et al., 2017). In this study, a history of cancer significantly increased the likelihood of developing breast cancer (OR=4.634, p=0.040). Histomorphological characteristics were significantly associated with breast cancer, with higher odds for lobular (OR=5.198, p=0.001) and ductal (OR=6.387, p=0.001) types. The study identified a history of cancer and specific histomorphological characteristics as the most critical risk factors.

Acknowledging the various risk factors is a critical milestone in averting the crises of the surging breast cancer cases. A history of cancer that had an odds ratio of 4.634, with close to five times the probability of breast cancer, is one of the most significant risk factors. Those with a history of cancer need to be considered as a substantial risk group that deserves to be closely monitored and screened for early detection of any potential tumors. Histomorphological patterns like fibroadenoma have a significant association with breast cancer and, therefore, need to be considered as an essential risk factor that would contribute to breast cancer. Other studies have also previously alluded that fibroadenoma could transform over time into malignancy.

Targeted patient management and therapy is a game changer in the management of the potential risk of breast cancer, with major priority, consideration, and attention given to those individuals at the highest risk. The higher the odds ratio, the higher the likelihood of developing breast cancer. In this study, the history of cancer and the histomorphological characteristics had the highest odds ratio, making them the most significant risk factors. Therefore, patients with a history of cancer or any histomorphological patterns require closer monitoring to avoid any potential threats of breast cancer.

#### **Implications for Practice**

The study found that late-stage diagnoses were prevalent, with 83.2% of malignant cases identified at stages III and IV, leading to poorer prognoses. Most malignant cases were Grade II (53.9%) and Grade III (32.3%), indicating more aggressive cancer types. Various benign conditions, such as fibroadenoma, could potentially develop into malignant tumors, emphasizing the need for vigilance in managing benign breast conditions. Educational and economic factors also played a significant role, with women having higher education levels showing lower frequencies of malignant conditions due to better health literacy and access to healthcare. Economic vulnerability hindered cancer care utilization, leading to

late diagnoses and poor health outcomes. The study's findings stress the importance of early detection, improved diagnostic methods, and addressing socioeconomic barriers to enhance breast cancer outcomes.

#### Conclusions

In conclusion, the study identified various histomorphological categories and patterns, including ductal, lobular, mixed, and others. The malignancy rates were 22.2% for the ductal category, 3.6% for lobular, 4.6% for mixed type, and 3.1% for others, resulting in an overall malignancy rate of 33.5%. Among these, 83.2% were late-stage cancers (stage III and IV). Fibroadenoma was the most prevalent benign histomorphological pattern at 33.0%, while lactating adenoma was the least common benign condition at 0.5%. Invasive ductal carcinoma was the most frequent malignant breast condition at 21.1%, with high-grade spindle cell carcinoma being the least common at 0.5%. The incidence of breast cancer in this study was notably higher at 33.5% in contrast to the national reported incidence of 16.1%.

The study also established associations between risk factors and histomorphological patterns in female patients suspected of breast cancer at KTRH. Among 194 patients, ages ranged from 15 to 91 years, with an intermediate age of 37 years and a median weight of 61.5 kg. Significant associations were found between tumor risk and factors such as age category, parity, history of cancer, histomorphological characteristics, and level of education. However, no significant associations were observed with alcohol consumption, hormonal contraceptives, or cigarette smoking. Histomorphological analysis revealed that certain conditions, like fibroadenoma and fibrocystic changes, were exclusively benign, while others, such as invasive ductal carcinoma, were exclusively malignant. The findings emphasize the importance of demographic and clinical factors in understanding breast cancer risks, highlighting key associations to inform targeted screening and interventions.

Furthermore, the study also deteremined the prevalent risk factors among female patients suspected of breast cancer at KTRH. It was found that a history of cancer significantly increased the likelihood of developing breast cancer (OR=4.634, p=0.040). Additionally, histomorphological characteristics were significantly associated with breast cancer, with lobular and ductal types showing higher odds (lobular: OR=5.198, p=0.001; ductal: OR=6.387, p=0.001). These findings underscore the importance of considering both medical history and histomorphological characteristics in assessing breast cancer risk, facilitating more targeted and effective screening and intervention strategies.

#### Recommendations from the current study

To address the high incidence of late-stage breast cancers, it is crucial to enhance early detection and screening programs through regular mammograms and breast exams, particularly for women over 40. Increasing community awareness and education on breast self-exams and clinical screenings, with a focus on recognizing early signs of breast cancer, is essential. Screening and preventive measures should be tailored to high-risk groups, including those with a family history of malignancy and those with low levels of education, and addressing barriers to accessing healthcare services. Implementation of a comprehensive cancer registry to monitor incidence and trends. Providing psychosocial support for patients and their families and developing personalized treatment protocols based on diverse histomorphological patterns are also recommended to improve overall treatment outcomes and quality of life.

The study recommends strengthening targeted screening programs based on its findings, particularly for women with higher risk factors such as specific age categories, lower parity, especially nulliparity, and a history of cancer. Public awareness and education campaigns should focus on early symptom recognition and the importance of regular screenings. Implementing risk-based screening protocols and improving access to genetic counseling for women with a family history of cancer is vital. Healthcare providers should receive training on the importance of demographic and clinical factors in assessing breast cancer risk. Prioritizing early intervention and treatment and establishing robust

data collection systems will enhance patient outcomes. Community-based programs and regular health check-ups should be promoted to increase accessibility and engagement, particularly in underserved areas.

Routine assessment and screening for those with benign histomorphological patterns, such as fibroadenoma, should be considered since they can transform into malignancy. There is a need for keen and precise consideration of the previous history of cancer to explore and ensure surveillance of the risk group.

#### **Recommendation for Further Studies**

- 1. Further studies should evaluate the effectiveness of enhanced early detection and screening programs, particularly for high-risk groups, and investigate barriers to healthcare access to improve early diagnosis. Research should also explore the influence of educational interventions on breast cancer awareness and assess personalized treatment protocols based on diverse histomorphological patterns.
- 2. Further studies should explore the effectiveness of targeted screening programs for women with identified higher risk factors, such as specific age categories, lower parity, and a history of cancer. Investigating the impact of public awareness campaigns on early symptom recognition and regular screenings is essential. Research should also assess the implementation of risk-based screening protocols and the role of genetic psychotherapy for women with a family history of cancer.
- **3.** Further studies should investigate the transformation potential of benign histomorphological patterns, such as fibroadenoma, into malignant forms to refine screening protocols. Additionally, research should focus on the effectiveness of routine assessments and screenings in individuals with a previous history of cancer to enhance surveillance and early detection in high-risk groups.

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#### Author Biodata

Anunda Job Marege is an academic researcher pursuing a master's in Histopathology and Cytology. With a primary background as a medical laboratory officer at Kisii Teaching and Referral Hospital, he brings 20 years of extensive experience in the field. Anunda's expertise spans various diagnostic and research techniques, significantly contributing to the understanding and awareness of breast cancer. His current research focuses on the histomorphological patterns and risk factors of breast cancer, aiming to inform better clinical practices and public health policies.

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